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10/565,083	01/18/2006	Tomoyuki Nishimoto	NISHIMOTO 8	5587
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BROWDY AND NEIMARK, P.L.L.C.			LAU, JONATHAN S	
624 NINTH STREET, NW				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**ADVISORY ACTION**

Continuation of 11.

Applicant's Remarks, filed 11 July 2008, have been fully considered and found not to be persuasive.

Applicant asserts that one of ordinary skill in the art would not have a reasonable expectation of success by treating 3- $\alpha$ -maltosyl  $\alpha,\alpha$ -trehalose even if Kubota teaches 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose. Applicant notes that the citation of Maruta at column 19, lines 37-40 disclose the treatment of a glycosyl trehalose using an amylase, in that case  $\beta$ -amylase, and not the case of using glucoamylase. Applicant is correct to point out that "glucoamylase" is a specific amylase with a specific enzymatic activity, and should be distinguished from other members of the family of amylases such as " $\alpha$ -amylase" and " $\beta$ -amylase". Examiner previously interpreted the term to encompass the family of amylases. Maruta does not specifically discloses the use glucoamylase to produce  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose at column 19, lines 37-40. Maruta does discloses the use of a selective amylase,  $\beta$ -amylase, to produce  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose at column 19, lines 37-40. However, the enzymatic activity of glucoamylase is well-known in the prior art and recognized within Maruta at column 19, lines 20-25 to act selectively on the  $\alpha$ -1,4 linkage and  $\alpha$ -1,6 linkage. As Kubota teaches a 3- $\alpha$ -glycosyl  $\alpha,\alpha$ -trehalose, with an  $\alpha$ -1,3 linkage, one of ordinary skill in the art would have a reasonable expectation of success in treating 3- $\alpha$ -maltosyl  $\alpha,\alpha$ -trehalose, because the selectivity of glucoamylase is well-known in the prior art and Maruta discloses the use of a selective amylase,  $\beta$ -amylase, to produce  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose at column 19, lines 37-40.

Continuation of 13. For purposes of appeal, an explanation of how the amended claims would be rejected is as provided below:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over as being unpatentable over Maruta et al. (US patent 6,017,899, issued 25 Jan 2000, of record) in view of Kubota et al. (WIPO publication WO 01/090338, published 29 Nov 2001, of record, English language equivalent US patent 7,192,746, of record). Herein citations of Kubota et al. refer to column and line numbers in US patent 7,192,746.

Maruta et al. discloses  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose, identified as PI, and  $\alpha$ -maltosyl  $\alpha,\alpha$ -trehalose, identified as PII. See column 19, line 52. Maruta et al. discloses a method of making non-reducing saccharides having a trehalose structure as an end unit using a saccharide-forming enzyme. See column 16, lines 64-67 and column 17, lines 1-5. Further, Maruta et al. teaches enzymatic hydrolysis by a selective amylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose and  $\alpha$ -maltosyl  $\alpha,\alpha$ -trehalose and teaches the selectivity of glucoamylase. See column 18 lines 57-67 and column 19 lines 37-40. Maruta et al. teaches a saccharide composition comprising trehalose and non-reducing saccharides consisting of one or more glucose molecules bound to one trehalose molecule via the  $\alpha$ -1,4 linkage or the  $\alpha$ -1,6 linkage and a member selected from the group consisting of foodstuffs, cosmetically acceptable materials, and pharmaceutically accepted materials. See claim 1 of Maruta et al. Maruta et al. further specify a food product in claim 8, a cosmetic in claim 9, and a pharmaceutical in claim 10.

Maruta et al. does not teach does not teach 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose (instant claim 3).

Kubota et al. teaches 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, which is a 3- $\alpha$ -glycosyl  $\alpha,\alpha$ -trehalose or a non-reducing saccharides having a trehalose structure as an end unit, and its method of making using a saccharide-transferring enzyme as either anticipated or obvious. See Kubota et al. column 44, lines 25-67. Kubota et al. teaches 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, a non-reducing saccharide consisting of four glucose units which differs from  $\alpha$ -maltosyl  $\alpha,\alpha$ -trehalose, a non-reducing saccharide consisting of

four glucose units, in the position of the  $\alpha$ -glycosidic bonds. See Kubota et al. column 44, lines 42-50.

It would have been obvious to combine the method of making non-reducing saccharides having a trehalose structure as an end unit using a saccharide-forming enzyme and enzymatic hydrolysis by glucoamylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose disclosed by Maruta et al. with 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose taught by Kubota et al. Maruta et al. discloses "a great demand for decreasing or even eliminating the reducing power of reducing partial starch hydrolysates without changing glucose units as a constituent saccharide thereof." See Maruta et al. column 2, lines 43-45. Maruta et al. disclose  $\alpha$ -maltosyl  $\alpha,\alpha$ -trehalose and  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose, a non-reducing saccharide consisting of three glucose units. In view of 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose disclosed by Kubota et al., 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose, a non-reducing saccharide consisting of three glucose units, instant claim 3 would have been obvious to one of ordinary skill in the art at the time of invention.

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 21 Dec 2007, with respect to the above ground of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant asserts that Kubota et al. does not teach the method for making 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, citing that Kubota et al. did not disclose the structure of the "glycosyl-transferred products" and that it was not known before the present invention was made that that 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose is produced when  $\alpha$ -isomaltosyl-

transferring enzyme is allowed to act on partial starch hydrolysate in the presence of trehalose as an acceptor.

"Where the claimed and prior art products ... are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. ... the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product." See MPEP 2112.01 I. As cited above (Kubota et al. column 44, lines 25-67), the prior art product is produced by identical or substantially identical processes. Therefore there is a *prima facie* case that Kubota et al. teaches 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose as "glycosyl-transferred products."

"Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. In re Rijckaert, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993)." See MPEP 2141.02 V. However, the process disclosed by Kubota et al. was known to make 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose prior to the time the instant invention was made. The  $\alpha$ -isomaltosyl-transferring enzyme disclosed by Kubota et al. is known in the prior art to catalyze the  $\alpha$ -1,3-intermolecular transglycosylation of the isomaltosyl residue onto a glucose group (column 43, lines 15-28). Therefore it would have been known that the process disclosed by Kubota et al. produced 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, the product of  $\alpha$ -1,3-intermolecular transglycosylation of the isomaltosyl residue onto  $\alpha,\alpha$ -trehalose, at the time of the instant invention was made.

Maruta et al. discloses enzymatic hydrolysis by glucoamylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose from non-reducing saccharides having a trehalose structure as an end unit. The combination of enzymatic hydrolysis by glucoamylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose from non-reducing saccharides having a trehalose structure as an end unit disclosed by Maruta et al. with the teaching of 3- $\alpha$ -glycosyl  $\alpha,\alpha$ -trehalose by Kubota et al., a non-reducing saccharides having a trehalose structure as an end unit, renders 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose obvious. The combination of Maruta et al. and Kubota et al. is motivated as disclosed by Maruta et al. of "a great demand for decreasing or even eliminating the reducing power of reducing partial starch hydrolysates without changing glucose units as a constituent saccharide thereof."

Amended Claims 10, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maruta et al. (US patent 6,017,899, issued 25 Jan 2000, of record) in view of Kubota et al. (WIPO publication WO 01/090338, published 29 Nov 2001, of record, English language equivalent US patent 7,192,746, of record). Herein citations of Kubota et al. refer to column and line numbers in US patent 7,192,746.

Maruta et al. discloses  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose, identified as PI (column 19, line 52). Maruta et al. discloses a method of making non-reducing saccharides having a trehalose structure as an end unit using a saccharide-forming enzyme (spanning column 16, lines 64-67 and column 17, lines 1-5). Maruta et al. discloses enzymatic hydrolysis by selective amylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose and the selectivity of glucoamylase (column 18 lines 57-67 and column 19 lines 37-40). Maruta et al.

teaches a saccharide composition comprising non-reducing saccharides consisting of one glucose molecule bound to one trehalose molecule and a member selected from the group consisting of foodstuffs (examples B-4 and B-5, column 31), cosmetically acceptable materials (example B-13 in column 33), and pharmaceutically acceptable materials (example B-14 spanning columns 33 and 34).

Maruta et al. does not teach does not teach the specific compounds 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose and 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose.

Kubota et al. teaches 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, which is a non-reducing saccharide having a trehalose structure as an end unit, and its method of making using an  $\alpha$ -isomaltosyl-transferring enzyme using trehalose and panose, O- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 6)-O- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 4)-D-glucose, a saccharide having a glucose polymerization degree of 3 and bearing  $\alpha$ -1,6 and  $\alpha$ -1,4 glucosidic bonds (column 44, lines 25-67).

It would have been obvious to combine the method of making non-reducing saccharides having a trehalose structure as an end unit using a saccharide-forming enzyme followed by enzymatic hydrolysis by glucoamylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose disclosed by Maruta et al. with the teaching of Kubota et al. of the method of making 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose using an  $\alpha$ -isomaltosyl-transferring enzyme, a method of making non-reducing saccharides having a trehalose structure as an end unit using a saccharide-forming enzyme. Maruta et al. discloses "a great demand for decreasing or even eliminating the reducing power of reducing partial starch hydrolysates without changing glucose units as a constituent saccharide thereof"

(Maruta et al. column 2, lines 43-45). Maruta et al. discloses production of  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose, a non-reducing saccharide consisting of three glucose units. Combining the teaching of making 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose by Kubota et al., a non-reducing saccharides having a trehalose structure as an end unit, with the process of Maruta et al. renders obvious the process for producing 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose by enzymatic reaction of glucoamylase. One of ordinary skill in the art at the time of the invention would have a reasonable expectation of success in combining Maruta et al. with the teaching of Kubota et al. to produce 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose because Maruta et al. discloses glucoamylase hydrolyzes  $\alpha$ -1,4 and  $\alpha$ -1,6 glycosidic bonds (Maruta et al. column 19, lines 20-23) and  $\beta$ -amylase hydrolyzes only  $\alpha$ -1,6 glycosidic bonds to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose (Maruta et al. column 19, lines 35-40).

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 21 Dec 2007, with respect to the above ground of rejection, has been fully considered and not found to be persuasive. Applicant asserts that Kubota et al. does not teach the method for making 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, citing that Kubota et al. did not disclose the structure of the "glycosyl-transferred products" and that it was not known before the present invention was made that that 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose is produced when  $\alpha$ -isomaltosyl-transferring enzyme is allowed to act on partial starch hydrolysate in the presence of trehalose as an acceptor.

"Where the claimed and prior art products ... are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. ... the *prima facie* case can be rebutted by evidence

showing that the prior art products do not necessarily possess the characteristics of the claimed product." See MPEP 2112.01 I. As cited above (Kubota et al. column 44, lines 25-67), the prior art product is produced by identical or substantially identical processes. Therefore there is a *prima facie* case that Kubota et al. teaches 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose as "glycosyl-transferred products."

"Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. In re Rijckaert, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993)." See MPEP 2141.02 V. However, there is evidence that supports the finding that the process disclosed by Kubota et al. was known to make 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose prior to the time the instant invention was made. The  $\alpha$ -isomaltosyl-transferring enzyme disclosed by Kubota et al. is known in the prior art to catalyze the  $\alpha$ -1,3-intermolecular transglycosylation of the isomaltosyl residue onto a glucose unit (Kubota et al. column 43, lines 15-28). Therefore it would have been known that the process disclosed by Kubota et al. produced 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose, the product of  $\alpha$ -1,3-intermolecular transglycosylation of the isomaltosyl residue onto a glucose unit of  $\alpha,\alpha$ -trehalose, at the time of the instant invention was made.

Applicant asserts that neither Kubota et al. nor Maruta et al. disclose the process for producing 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose by enzymatic reaction of glucoamylase. As recited above, Maruta et al. discloses enzymatic hydrolysis of non-reducing saccharides having a trehalose structure as an end unit by glucoamylase to generate  $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose. Maruta et al. does not specifically disclose this process using 3- $\alpha$ -glucosyl

$\alpha,\alpha$ -trehalose. Kubota et al. remedies the deficiency of Maruta et al. by teaching 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose. Combining the teaching of 3- $\alpha$ -isomaltosyl  $\alpha,\alpha$ -trehalose by Kubota et al., a non-reducing saccharides having a trehalose structure as an end unit, with the process of Maruta et al. renders obvious the process for producing 3- $\alpha$ -glucosyl  $\alpha,\alpha$ -trehalose by enzymatic reaction of glucoamylase.

/Shaojia Anna Jiang, Ph.D./

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